

**REMARKS**

In the final Office Action mailed March 24, 2005, claims 105-112 and 115-125, 127-132 and 134 were rejected under 35 U.S.C. §103(a) as obvious over US Pat. No. 5,395,825 - ("Feinberg"), in view of Lea *et al.*, Nocera *et al.*, Clark *et al.*, Thomas *et al.*, Thaler *et al.*, and Prakash *et al.* Claims 113 and 114 were rejected as obvious over Feinberg, in view of Lea *et al.*, Nocera *et al.*, Clark *et al.*, Thomas *et al.*, Thaler *et al.*, and Prakash *et al.*, Harlow *et al.*, and Martin-Villa *et al.* Claim 126 was rejected as obvious over Feinberg, in view of Lea *et al.*, Nocera *et al.*, Clark *et al.*, Thomas *et al.*, Thaler *et al.*, Prakash *et al.*, and Grainger *et al.*, and claim 133 was rejected as obvious over Feinberg, in view of Lea *et al.*, Nocera *et al.*, Clark *et al.*, Thomas *et al.*, Thaler *et al.*, Prakash *et al.*, and Heidenreich *et al.* The specific grounds for rejection, and applicant's response thereto, are set out in detail below.

Claims 105-134 were pending at the issuance of the March 24, 2005 Office Action. Claims 1-104 and 135-140 previously were canceled. Claims 115, 120, 123, and 128-131 are canceled herein, claims 105-109, 112, 113, 116-119, 121, 122, 124-127, 132-132-134 have been amended and claims 141 to 144 have been added. The amendments to the claims are fully supported by the specification. Support for the amendment to claim 105 is found in canceled claim 130. Support for added claim 141 is found in canceled claim 128, support for added claim 142 is found in canceled claim 129, support for added claim 143 is found in canceled claim 120, and support for added claim 144 is found in canceled claim 123. Applicants submit that the added claims recite the limitations previously recited in now-canceled claims 120, 123, and 128-130 and therefore require no additional search and place no additional burden on the examiner. As described below, the previous examiner deemed that the subject matter of claims 105, and 141-144 was free of the prior art. Applicants further submit that the amended claims require no further search and place the claims in condition for allowance and, accordingly, request entry of the amendments presented herein.

Claims 105-114, 116-119, 121, 122, 124-127, 132-134 and 141-144 are pending for consideration, which is respectfully requested in view of the foregoing amendments and following remarks.

**Rejection under §103(a)**

Claims 105-125 and 127-140 are rejected under 35 U.S.C. §103(a) as obvious over US Pat. No. 5,395,825 - ("Feinberg"), in view of Lea *et al.*, Nocera *et al.*, Clark *et al.*, Thomas *et al.*, Thaler *et al.*, and Prakash *et al.* Claims 113 and 114 are rejected as obvious over Feinberg in view of Lea, Nocera, Clark, Thomas, Thaler, Prakash, Harlow *et al.*, and Martin-Villa *et al.* The Examiner has also rejected claim 126 as obvious over Feinberg, in view of Lea, Nocera, Clark, Thomas, Thaler, Prakash, and Grainger *et al.* and claim 133 as obvious over Feinberg, in view of Lea, Nocera, Clark, Thomas, Thaler, Prakash, and Heidenreich *et al.*

The Examiner asserts that Feinberg differs from the claimed invention "only in that the method of treating infertility by inducing immune tolerance by exposing [a] mucosal surface of [the] prospective mother with semen or MHC class I antigen of a prospective father capable of eliciting a Th-1 response[,] and substantially purified TGF $\beta$ ." Applicants respectfully submit that this statement fails to specify the perceived differences between Feinberg and the instantly claimed invention. Nevertheless, applicants understand the Examiner's argument to be that the claimed invention would have been obvious in view of new combinations of the cited art. Applicants respectfully traverse the rejection because none of the references, either alone or in combination, teaches or suggests the instantly claimed invention. Specifically, none of the cited references teaches or suggests methods of treating recurrent miscarriage by inducing immune tolerance to a paternal antigen in a prospective mother by exposing a mucosal surface of the prospective mother to (1) semen or an MHC Class I antigen of a prospective father and (2) a substantially purified TGF $\beta$ , wherein the exposure is at the time or in the dosage recited in the instant claims.

All claims are presumed initially to be non-obvious. A *prima facie* case of obviousness requires three elements: (1) a teaching or suggestion of all of the claim limitations; (2) a suggestion or motivation to modify or combine the teachings of the applied prior art; and (3) a reasonable expectation of success in reaching the claimed invention. The Examiner bears the initial burden of supporting any *prima facie* assertion of obviousness with adequate facts. MPEP § 2142 (Feb. 2000). Applicants respectfully submit that the Examiner has failed to provide adequate facts to support a *prima facie* case of obviousness here.

Applicants submit that nowhere in the prior art, alone or in combination, is the suggestion or teaching of the specific delivery times or dosages present in applicants' pending claims. In support of this statement, applicants point out that in the Office Actions dated August 27, 2002, March 11, 2003, and January 16, 2004 the dependent claims encompassing the exact same delivery times and dosages were deemed as being "free of the prior art." Applicants note that no new prior art documents have been cited since the subject matter of those claims were deemed free of prior art. Because applicants have amended the claims to include subject matter that was previously deemed free of prior art, applicants submit that the amended claims should be in condition for allowance. As such, withdrawal of the rejection respectfully is requested.

Moreover, applicants note that the primary reference (Feinberg) teaches away from the instantly claimed invention. Specifically, Feinberg claims that failure of a conceptus to implant in the uterus can be addressed by administering a very low dose of TGF $\beta$  simultaneously with the conceptus in an IVF procedure. The TGF $\beta$  is alleged to increase fibronectin production in the uterus thereby permitting implantation of the conceptus.

The instant claims recite methods of preventing miscarriage of an implanted conceptus by inducing maternal tolerance to the implanted conceptus by administering (1) paternal antigens and (2) TGF $\beta$ , where the TGF $\beta$  is administered at much higher dosages and in a dosing regimen, suitable for inducing tolerance. Both the dosage and dosage regimen of the TGF $\beta$  administration recited in the instant claims are quite distinct from those taught or suggested by Feinberg. Moreover, nothing in Feinberg teaches or suggests that inducing maternal tolerance would be in any way useful for preventing miscarriage and therefore there would not have been any motivation for one skilled in the art to have modified the dosages or dosing regimen suggested by Feinberg to arrive at the methods recited in the instant claims.

In sum, Feinberg fails to teach or suggest the instantly claimed methods and the secondary references fail to remedy the deficiencies of Feinberg. Even when considered in combination, the cited prior art does not suggest or teach the claimed subject matter. Accordingly, withdrawal of the rejection respectfully is requested.


### CONCLUSION

Applicants respectfully assert that the amendments presented above should be entered as they place this case in condition for allowance by clarifying the invention and responding the Examiner's suggestions or concerns. In view of the amendment and remarks, applicants respectfully request that all objections and rejections be withdrawn and that a notice of allowance be forthcoming. The Examiner is invited to contact the undersigned attorney for applicants at (202) 912-2197 for any reason related to the advancement of this case.

Respectfully submitted,

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